



MAP3K1 gene

mitogen-activated protein kinase kinase kinase 1

Normal Function

The *MAP3K1* gene provides instructions for making a protein that helps regulate signaling pathways that control various processes in the body, including the processes of determining sexual characteristics before birth. The MAP3K1 protein attaches (binds) to other molecules called RHOA, MAP3K4, FRAT1, and AXIN1. The binding of MAP3K1 to these molecules, which are called cofactors, helps MAP3K1 control the activity of the signaling pathways.

Health Conditions Related to Genetic Changes

breast cancer

Langerhans cell histiocytosis

Swyer syndrome

Mutations in the *MAP3K1* gene are thought to account for up to 18 percent of cases of Swyer syndrome, a condition affecting sexual development also known as 46,XY complete gonadal dysgenesis or 46,XY pure gonadal dysgenesis.

People usually have 46 chromosomes in each cell. Two of the 46 chromosomes, known as X and Y, are called sex chromosomes because they help determine whether a person will develop male or female sex characteristics. Girls and women typically have two X chromosomes (46,XX karyotype), while boys and men usually have one X chromosome and one Y chromosome (46,XY karyotype).

The *MAP3K1* gene mutations that cause Swyer syndrome increase cofactor binding, which decreases signaling that leads to male sexual differentiation and enhances signaling that leads to female sexual differentiation. As a result, affected individuals with a typically male 46,XY karyotype will not develop male gonads (testes) but will develop female reproductive structures (a uterus and fallopian tubes).

other disorders

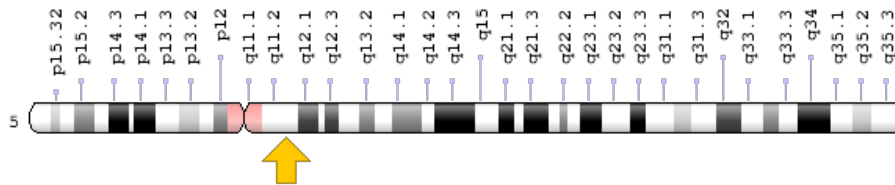
MAP3K1 gene mutations have also been identified in people with 46,XY disorder of sex development, which is also known as partial gonadal dysgenesis. These mutations likely have similar but less pronounced effects on signaling related to sexual development than those that cause Swyer syndrome (described above). Affected individuals may have external genitalia that do not look clearly male or

clearly female (ambiguous genitalia) or other abnormalities of the genitals and reproductive organs.

Chromosomal Location

Cytogenetic Location: 5q11.2, which is the long (q) arm of chromosome 5 at position 11.2

Molecular Location: base pairs 56,815,073 to 56,896,152 on chromosome 5 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- M3K1_HUMAN
- MAP/ERK kinase kinase 1
- MAPK/ERK kinase kinase 1
- MAPKKK1
- MEK kinase 1
- MEKK
- MEKK 1
- MEKK1
- mitogen-activated protein kinase kinase kinase 1, E3 ubiquitin protein ligase
- SRXY6

Additional Information & Resources

Educational Resources

- Endotext: Sex Determination
https://www.ncbi.nlm.nih.gov/books/NBK279001/#_sex-differentiation_toc-sex-determination_

GeneReviews

- Nonsyndromic Disorders of Testicular Development
<https://www.ncbi.nlm.nih.gov/books/NBK1547>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28MAP3K1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D>

OMIM

- 46,XY SEX REVERSAL 6
<http://omim.org/entry/613762>
- MITOGEN-ACTIVATED KINASE KINASE KINASE 1
<http://omim.org/entry/600982>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_MAP3K1.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=MAP3K1%5Bgene%5D>
- HGNC Gene Family: Mitogen-activated protein kinase kinase kinases
<http://www.genenames.org/cgi-bin/genefamilies/set/654>
- HGNC Gene Family: Zinc fingers SWIM-type
<http://www.genenames.org/cgi-bin/genefamilies/set/90>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=6848
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/4214>
- UniProt
<http://www.uniprot.org/uniprot/Q13233>

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